

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representation of
The original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification:
G01N 21/77, G01N 21/55

A1 (11) International Publication Number:
(43) International Publication Date:

WO 00/23793
27 April 2000 (27.04.2000)

(21) International Application Number: PCT/US99/20689

Published

(22) International Filing Date: 09 September 1999 (09.09.1999)

(30) Priority Data:
09/174,178 16 October 1998 (16.10.1998) US

(60) Parent Application or Grant

IMATION CORP. []; (i) CHALLENGER, William, A. [];
(i) DEPUYDT, James, M. []; (i) TOLBERT, William, A. [];
(i) LEVENS, Eric, D. [].

(54) Title: OPTICAL SENSOR HAVING DIELECTRIC FILM STACK

(54) Titre: CAPTEUR OPTIQUE COMPORTANT UN EMPILEMENT DE COUCHES DIELECTRIQUES

(57) Abstract

A method and apparatus (100) for optically assaying a targeted substance in a sample using a sensor (50) comprising a dielectric film stack having a plurality of dielectric layers. For at least one angle of incidence the dielectric layers (52, 54, 58) operate as a waveguide for light incident upon the sensor. In one configuration, each dielectric layer comprises a dielectric material selected from a first dielectric material having a first index of refraction and a second dielectric material having a second index of refraction. The dielectric film stack is formed such that the dielectric material of the dielectric layers alternates between the first dielectric material and the second dielectric material. The dielectric film stack is either formed as a dielectric mirror such that light incident upon the sensor reflects from the sensors or as an anti-reflection film stack, such that light incident upon the light beam propagates through the sensor. The inventive sensor exhibits a resonance that is comparable in magnitude with resonances commonly exhibited by conventional SPR sensors. However, unlike grating-based SPR sensors, the inventive sensor allows a sample (21) to be assayed with substrate-incident light such that the incident light need not propagate through the sample. In addition, because the sensor does not rely on the use of conductive metals, the sensor enables sharp resonances at short wavelengths than conventional SPR sensors.

(57) Abrégé

L'invention concerne un procédé et un dispositif (100) qui permettent d'analyser optiquement une substance contenue dans un échantillon au moyen d'un capteur (50) comprenant un empilement de couches diélectriques (52, 54, 58) constitué d'une pluralité de couches diélectriques. Pour au moins un angle d'incidence, les couches diélectriques tiennent lieu de guide d'onde pour la lumière tombant sur le capteur. Dans l'une des configurations, chaque couche diélectrique comprend un matériau diélectrique choisi entre un premier matériau diélectrique ayant un premier indice de réfraction et un second matériau diélectrique ayant un second indice de réfraction. L'empilement de couches diélectriques est tel que les couches diélectriques sont constituées alternativement du premier matériau diélectrique et du second matériau diélectrique. L'empilement se présente soit sous forme de miroir diélectrique, de façon que la lumière tombant sur le capteur soit réfléchi par celui-ci, soit comme un empilement anti-réfléchissant, de façon que la lumière tombant sur le capteur se propage à travers lui. Le capteur de l'invention possède une amplitude de résonance comparable aux résonances habituelles des capteurs à résonance plasmonique de surface (SPR) classiques. Cependant, à la différence des capteurs SPR à base de réseau de diffraction, il permet d'analyser un échantillon (21) avec une lumière qui tombe sur le substrat sans être obligée de se propager à travers l'échantillon. En outre, du fait qu'il ne fait pas appel à des métaux conducteurs, il permet des résonances pointues à des longueurs d'onde plus courtes que les capteurs SPR classiques.

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



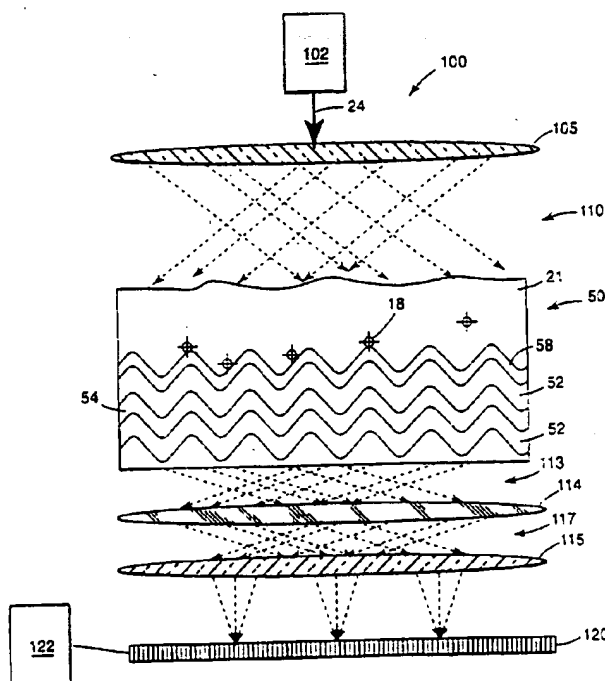
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7: G01N 21/77, 21/55		A1	(11) International Publication Number: WO 00/23793
(21) International Application Number: PCT/US99/20689		(43) International Publication Date: 27 April 2000 (27.04.00)	
(22) International Filing Date: 9 September 1999 (09.09.99)		(81) Designated States: CN, JP, KR, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(30) Priority Data: 09/174,178 16 October 1998 (16.10.98) US		Published With international search report. With amended claims and statement.	
(71) Applicant: IMATION CORP. [US/US]; 1 Imation Place, P.O. Box 64898, Saint Paul, MN 55164-0898 (US).			
(72) Inventors: CHALLENGER, William, A.; P.O. Box 64898, Saint Paul, MN 55164-0898 (US); DEPUYDT, James, M.; P.O. Box 64898, Saint Paul, MN 55164-0898 (US); TOLBERT, William, A.; P.O. Box 64898, Saint Paul, MN 55164-0898 (US).			
(74) Agents: LEVINSON, Eric, D. et al.; Imation Corp., Imation Legal Affairs, P.O. Box 64898, Saint Paul, MN 55164-0898 (US).			

(54) Title: OPTICAL SENSOR HAVING DIELECTRIC FILM STACK

(57) Abstract

A method and apparatus (100) for optically assaying a targeted substance in a sample using a sensor (50) comprising a dielectric film stack having a plurality of dielectric layers. For at least one angle of incidence the dielectric layers (52, 54, 58) operate as a waveguide for light incident upon the sensor. In one configuration, each dielectric layer comprises a dielectric material selected from a first dielectric material having a first index of refraction and a second dielectric material having a second index of refraction. The dielectric film stack is formed such that the dielectric material of the dielectric layers alternates between the first dielectric material and the second dielectric material. The dielectric film stack is either formed as a dielectric mirror such that light incident upon the sensor reflects from the sensors or as an anti-reflection film stack such that light incident upon the light beam propagates through the sensor. The inventive sensor exhibits a resonance that is comparable in magnitude with resonances commonly exhibited by conventional SPR sensors. However, unlike grating-based SPR sensors, the inventive sensor allows a sample (21) to be assayed with substrate-incident light such that the incident light need not propagate through the sample. In addition, because the sensor does not rely on the use of conductive metals, the sensor enables sharp resonances at short wavelengths than conventional SPR sensors.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

Description

5

10

15

20

25

30

35

40

45

50

55

OPTICAL SENSOR HAVING DIELECTRIC FILM STACK

Field of the Invention

This invention relates generally to the field of optical assaying, and more particularly to an optical sensor having a dielectric film stack.

Background of the Invention

Extremely sensitive optical sensors have been constructed by exploiting an effect known as surface plasmon resonance (SPR). These sensors are capable of detecting the presence of a wide variety of materials in concentrations as low as picomoles per liter. SPR sensors have been constructed to detect many biomolecules including keyhole limpet hemocyanin, α -fetoprotein, IgE, IgG, bovine and human serum albumin, glucose, urea, avidin, lectin, DNA, RNA, HIV antibodies, human transferrin, and chymotrypsinogen. Additionally, SPR sensors have been built which detect chemicals such as polyazulene and nitrobenzenes and various gases such as halothane, trichloroethane and carbon tetrachloride.

An SPR sensor is constructed by sensitizing a surface of a substrate to a specific substance. Typically, the surface of the substrate is coated with a thin film of metal such as silver, gold or aluminum. Next, a monomolecular layer of sensitizing material, such as complementary antigens, is covalently bonded to the surface of the thin film. In this manner, the thin film is capable of interacting with a predetermined chemical, biochemical or biological substance. When an SPR sensor is exposed to a sample that includes a targeted substance, the substance attaches to the sensitizing material and changes the effective index of refraction at the surface of the sensor. Detection of the targeted substance is accomplished by observing the optical properties of the surface of the SPR sensor.

There are two common constructions of an SPR sensor. Figure 1 illustrates a prism-based SPR sensor 10 that is the most common form of SPR sensors. Sensor 10 includes a disposable slide 20 that is placed on a fixed glass prism 12. Slide 20 is coated with a metal film 16 and sensitizing material 22 is capable of interacting with target substance 18 in sample 21. Before placing slide

5 20 on prism 12, an operator coats prism 12 with an anti-reflection coating 14, often a fluid, in order to prevent light beam 24 from reflecting before reaching metal-film layer 16.

10 Light source 28 generates light beam 24 that is incident upon sensor 10. Sensor 10 reflects light beam 24 as light beam 26 received by detector 30. At a specific angle of incidence of light beam 24, known as the resonance angle, a very efficient energy transfer and excitation of the surface plasmon occurs in metal film 16. As a result, reflected light 26 exhibits an anomaly, such as a sharp attenuation, and the resonance angle of sensor 10 can be readily detected. When 15 targeted substance 18 attaches to sensitizing material 22, a shift in the resonance angle occurs due to the change in the refractive index at the surface of sensor 10. A quantitative measure of the concentration of targeted substance 18 can be calculated according to the magnitude of shift in the resonance angle.

25 A second common form of an SPR sensor, known as grating-based SPR sensor, involves the use of a metal diffraction grating instead of glass prism. Figure 2 illustrates a grating-based SPR sensor 40 in which substrate 45 is formed to have sinusoidal grooves. In grating-based SPR sensors, the period of the groove profile of substrate 45 typically ranges from 0.4 μm to 2.0 μm . Thin 30 metal film 42 is formed outwardly from the surface of substrate 45 and comprises any suitable metal such as aluminum, gold or silver. In one embodiment, layer 42 comprises silver having a thickness of approximately 100 nm.

35 Sensitizing layer 44 is formed outwardly from metal film 42. Sensitizing layer 44 is selected to interact with a predetermined chemical, biochemical or biological substance 18 contained in sample 21. In one embodiment, sensitizing 40 layer 44 comprises a layer of antigens capable of trapping a complementary antibody. Recently, several techniques have been developed for attaching antigens as a receptive material to film 42 such as spin coating with a porous silica-sol-gel or a hydrogel matrix. Preferably, sensitizing layer 44 is less than 100 nm thick.

45 In Figure 2, light source 28 produces light beam 24 incident upon sensor 40 such that detector 30 receives reflected light beam 26. For grating-based SPR 50

5 sensors, resonance occurs, and reflected light beam 26 exhibits an anomaly, when
a polarization component of light beam 24 is perpendicular to the groove
10 direction of the surface of substrate 45 and the angle of incidence of light beam
24 is appropriate for energy transfer and excitation of the surface plasmon in thin
5 metal film 42.

Grating-based SPR sensors have several distinct advantages over prism-
15 based SPR sensors. For example, the resonance angles of grating-based SPR
sensors may be finely tuned by adjusting the groove profile. In addition, grating-
based SPR sensors do not require the use of an anti-reflection coating. Grating-
10 based SPR sensors, however, suffer from the fact that the light must propagate
through the sample as opposed to prism-based sensors in which the incident light
20 propagates through the prism and strikes the metal film opposite from the sample.
Propagation through the sample is disadvantageous because the sample tends to
absorb or scatter the incident light. For these reasons, grating-based SPR sensors
25 are ill suited for assaying liquids, such as blood, and are primarily used in gas
sensing applications. Furthermore, both of the above-described SPR sensors rely
on a highly conducting metallic film to support the surface plasmon resonance.
30 This metal film, however, limits the wavelength of the resonance to the red or
infrared region of the light spectrum because at shorter wavelengths the
20 conductivity of even the best metals is not sufficient to generate sharp resonances,
thereby resulting in lower sensitivity.

For the reasons stated above, and for other reasons stated below which
will become apparent to those skilled in the art upon understanding the present
invention, there is a need in the art for an optical sensor having the benefits of
40 grating-based SPR sensor that does not require that the incident light propagate
25 through the sample.

45 Summary of the Invention

Described herein is a method and apparatus for optically assaying a
30 targeted substance in a sample using an inventive sensor that overcomes the
above-described deficiencies of conventional grating-based and prism-based SPR
50

5 sensors. The sensor exhibits a sharp resonance that is comparable in magnitude with resonances commonly exhibited by conventional SPR sensors. However, unlike grating-based SPR sensors, a sample may be assayed by reflectance from
10 the substrate side without propagating light through the sample. In addition, the sensor allows a sample to be assayed with transmitted light. One advantage of assaying with transmitted light is the ability to use a diffused light source.
15 Because the sensor does not rely on the use of conductive metals, the sensor enables sharp resonances at shorter wavelengths than conventional SPR sensors.

According to one aspect, the invention is a sensor comprising a dielectric
10 film stack having a plurality of dielectric layers. The dielectric layers operate as a waveguide such that a portion of the incident light propagates within the dielectric film stack for at least one angle of incidence. In one embodiment, the dielectric layers are formed with a dielectric material selected from either a first
20 dielectric material having a first index of refraction or a second dielectric material having a second index of refraction. In one configuration, the dielectric film stack is formed such that the dielectric material of the dielectric layers alternates
25 between the first dielectric material and the second dielectric material. The dielectric film stack may be formed as a dielectric mirror, such that light incident upon the sensor substantially reflects from the sensor, or as an anti-reflection film
30 stack such that incident light is transmitted through the sensor with substantially no reflection.

According to another aspect, the invention is a sensing system including a
35 sensor having a stack of dielectric layers. A light source exposes the sensor with a light beam. The dielectric layers of the sensor operate as a waveguide such that
40 a portion of the incident light propagates within the dielectric film stack for at least one angle of incidence. A detector receives light from the sensor and produces an output signal representative of an intensity of the received light. A
45 controller is coupled to the detector and calculates a measure of the substance in the sample as a function of the output signal. In one embodiment a diffuser
50 diffuses the incident light beam from the light source and a lens focuses the light transmitted through the sensor onto a corresponding element of the detector

array according to a transmission angle.

According to yet another aspect, the invention is a method for assaying a targeted substance in a sample. A sensor is interacted with the sample having a targeted substance. The sensor comprises a dielectric film stack having a plurality of dielectric layers that operate as a waveguide for incident light. A measure of the targeted substance in the sample is determined as a function of a shift in a detected optical anomaly exhibited by light received from the sensor. In one embodiment, the measure is determined by detecting an optical anomaly in light reflected by the sensor. In another embodiment, the measure includes detecting an optical anomaly in light transmitted through the sensor.

These and other features and advantages of the invention will become apparent from the following description of the preferred embodiments of the invention.

Brief Description of the Drawings

Figure 1 is a schematic side view of a sensing system having a prism-based surface plasmon resonance sensor;

Figure 2 is a schematic side view of a sensing system having a grating-based surface plasmon resonance sensor;

Figure 3 is a cross-sectional view of one embodiment of an optical sensor having a dielectric film stack in accordance with the present invention; and

Figure 4 is a schematic side view of one embodiment of a sensing system for assaying a substance in a sample by exposing a sensor having a dielectric film stack and detecting a shift in one or more resonance angles.

Detailed Description

In the following detailed description, references are made to the accompanying drawings that illustrate specific embodiments in which the invention may be practiced. Electrical, mechanical and structural changes may be made to the embodiments without departing from the spirit and scope of the present invention. The following detailed description is, therefore, not to be

5 taken in a limiting sense and the scope of the present invention is defined by the appended claims and their equivalents

10 Figure 3 is a cross-sectional profile of an optical sensor 50 formed in accordance to the present invention. It is observed that an optical sensor may be
5 constructed which exhibits resonance angles comparable to conventional SPR sensors but which overcomes many of the above-described disadvantages. More specifically, the inventive sensor 50 uses a dielectric film stack instead of a thin
15 metal film. Sensor 50 includes substrate 51 having surface 53 formed with sinusoidal grooves. The period of the groove profile of surface 53 may range
10 from less than 0.4 μm to over 2.0 μm . Other groove profiles, such as trapezoidal, square, etc., are also well suited for the invention.

20 Formed outwardly from surface 53 of substrate 51 is a plurality of transparent dielectric layers 52 that collectively form a dielectric film stack on surface 53 of substrate 51. Although illustrated as such, dielectric layers 52 need
25 not conform to the surface profile of substrate 51. As described in detail below, sensor 50 exhibits sharp resonances that are comparable in magnitude with resonances commonly seen in SPR sensors. In one embodiment, dielectric layers
30 52 of the dielectric film stack are configured to operate as a dielectric mirror that reflects substantially all of light beam 62 at non-resonance angles. More specifically, each dielectric layer 52 of the dielectric film stack reflects a portion
35 of light beam 62 as light beam 66. This embodiment is advantageous because, unlike grating-based SPR sensors, sample 21 may be assayed using substrate-incident light beam 62 such that the light beam 62 need not propagate through sample 21. In another embodiment, sensor 50 is not constructed as a dielectric
40 mirror but as an anti-reflection film stack. In this configuration, at non-resonance angles light beam 62 transmits through sensor 50 with substantially no diffusion or reflection and emerges as light beam 64. In this manner, the dielectric film stack of sensor 50 operates exactly opposite when it is formed as an anti-
45 reflection dielectric film stack than when it is formed as a dielectric mirror. Configuration of the dielectric film stack for operation as either a dielectric mirror
30 or as an anti-reflection film stack is discussed in detail below.

5 Regardless of whether the dielectric film stack is configured to operate as
a dielectric mirror or an anti-reflection film stack, at the resonance angles the
dielectric film stack operates as a waveguide such that reflected light beam 66 and
10 transmitted light beam 64 exhibit sharp anomalies. At the resonance angles
5 energy is transferred from light beam 62 to dielectric layers 52 of the dielectric
film stack such that dielectric layers 52 collectively act as a waveguide. When
dielectric layers 52 collectively operate as a waveguide a finite portion of incident
15 light beam 62 propagates within the dielectric film stack. If the dielectric film
stack is constructed as a dielectric mirror, the remaining light not propagating
10 within the dielectric film stack transmits through sensor 50 and emerges as light
beam 64, thereby causing a sharp attenuation in reflected light 66 and a sharp
20 increase in transmitted light 64. If, however, the dielectric film stack is
constructed as an anti-reflection film stack, the remaining light is reflected as light
beam 66, thereby causing a sharp attenuation in transmitted light 64 and a sharp
25 increase in reflected light 66.

 Sensitizing layer 58 is formed outwardly from outermost dielectric layer
52 and is selected to interact with a predetermined chemical, biochemical or
30 biological substance 18 contained in sample 21. When targeted substance 18
attaches to sensitizing layer 58, a shift in the resonance angles occurs due to the
20 change in the refractive index of sensor 50. A quantitative measure of the
concentration of targeted substance 18 can be calculated according to the
35 magnitude of shift in the resonance angle by monitoring either reflected light 66
or transmitted light 64. Thus, one advantage of sensor 50 over conventional SPR
sensors is that sensor 50 can be used in reflection-based sensing systems or
40 transmission-based sensing systems.

 In one embodiment the dielectric film stack is configured to operate as a
dielectric mirror by forming each dielectric layer with a dielectric material
45 selected from a first dielectric material and a second dielectric material. The first
dielectric material has a first index of refraction while the second dielectric
30 material has a second index of refraction. In one particularly advantageous
configuration, the stack of dielectric layers is formed such that the dielectric
50

material of the dielectric layers alternates between the first dielectric material and the second dielectric material. For example, in one embodiment, dielectric materials of dielectric layers 52 are selected such that dielectric layers 52₁ and 52₃ have a high index of refraction while dielectric layer 52₂ has a low index of refraction. This configuration is advantageous because the magnitude of the anomalies exhibited by light beams 64 and 66 are substantial and more readily detectable, thereby increasing the sensitivity of sensor 50.

As light beam 62 penetrates the dielectric film stack of sensor 50, a portion of light beam 62 is reflected at each dielectric layer 52. More specifically, as light beam 62 penetrates a given dielectric layer 52, a portion of the light is reflected at the surface of the next dielectric layer 52. As such, when light beam 62 is incident normal to the dielectric film stack, the total distance traveled within any given dielectric layer is approximately twice the thickness, t , of the dielectric layer, i.e., $2t$. In order to form the dielectric film stack as a dielectric mirror such that light beam 62 is substantially reflected from sensor 50 as light beam 66, each dielectric layer 52 is formed with an approximate thickness t defined by the following equation:

$$t = \frac{\lambda}{4n} + \frac{m \cdot \lambda}{2n}$$

where λ is the wavelength of light beam 62, n is the index of refraction of the dielectric layer being formed and m is any positive integer. For other angles of incidence, this equation is easily modified.

When each dielectric layer is formed according to the above equation, and m equals zero, the total distance traveled within a given dielectric layer is $\lambda/2n$. This corresponds to a total "optical" distance traveled within each dielectric layer of one half of the wavelength of the light, $\lambda/2$, which corresponds to a retardation of 180°.

At the reflecting surface there is an additional 180° of retardation if the penetrated dielectric layer has a high index of refraction, n , and the next dielectric layer has a low index. Therefore, for each of these high index/low index

5 interfaces, reflected light beam 66 undergoes a total retardation of 360° and
returns to the surface of the penetrated dielectric layer 52 in phase with the
portion of light beam 66 reflected from that surface. When the dielectric film
10 stack is formed according to the above equation and dielectric layers 52 alternate
5 between a high index and a low index, all the internally reflected light beam 66
are in phase, thereby causing constructive interference that results in substantial
reflectivity. For example, according to this configuration, sensor 50 can be
15 constructed to reflect at least 50%, or even at least 90%, of light beam 62. The
dielectric film stack acts as a dielectric mirror when the dielectric layers are
10 formed according to the above equation for any positive integer m . As m
increases, the thickness t increases by $\lambda/2$ such that the total "optical" distance
20 traveled within a dielectric layer increases by one full wavelength λ , thereby
resulting in interference and substantial reflectivity of light beam 62.

25 In one embodiment, the dielectric material used for one set of the
alternating dielectric layers, such as dielectric layers 52₁ and 52₃, is selected to
have the highest index of refraction of any dielectric material that can be formed
on sensor 50. For example, titanium dioxide, TiO_2 , is a suitable dielectric
30 material because it has an index of refraction equaling approximately 2.5. The
dielectric material used for the other dielectric layers, such as dielectric layers 52₂,
20 is selected to have the lowest index of refraction of any dielectric material that
can be formed on sensor 50. For example, silicon dioxide, SiO_2 , is a suitable
35 dielectric material because it has an index of refraction equaling approximately
1.5. Selecting the dielectric materials for dielectric layers 52 as such provides a
dielectric mirror having high reflectivity, often approaching 90%, for most angles
40 yet exhibiting sharp attenuation at the resonance angles, often approaching 0%
25 reflected light. Furthermore, a suitable dielectric material for dielectric layer 52₂
may have a corresponding index of refraction approaching 1.8. Similarly, a
45 suitable dielectric material for dielectric layers 52₁ and 52₃ may have a
corresponding index of refraction of at least 2.2. In addition, the magnitude of
50 the exhibited anomaly increases as the number of dielectric layers increases;
however, the magnitude of the angular shift tends to decrease. Therefore a

5 balance between these two characteristics must be determined. Although other numbers of layers are acceptable, experiments suggest that five to fifteen dielectric layers provide good results with eleven layers working particularly well.

10 In order for the dielectric film stack of sensor 50 to operate as a dielectric mirror it is not necessary that the dielectric film stack be formed from two alternating dielectric layers. A dielectric layer mirror can also be constructed with dielectric layers having several different indices of refraction. In this case it is important that the thickness of each layer be described by the previous equation. In addition, each layer must be bounded by other layers that both have either a
15 higher refractive index or a lower refractive index. For example, the dielectric film stack may be formed from three dielectric materials with indices n_1 , n_2 , n_3 where $n_1 < n_2 < n_3$. A suitable dielectric film stack formed from these materials could be constructed by following the sequence of dielectric indexes:

20 $n_3, n_2, n_3, n_1, n_2, n_1, n_3, n_2, n_3$.

25 As described above, the dielectric film stack of sensor 50 can be constructed to operate as an anti-reflection dielectric film stack. Although there is no general equation that can be given for designing anti-reflection film stacks, an iterative approach using computer modeling may be used. Following this approach, one example of an antireflecting dielectric film stack is TiO_2 , SiO_2 and
30 TiO_2 deposited on a glass substrate for which the index of refraction of the TiO_2 layers is 2.5 and the index of refraction of the SiO_2 layer and the glass substrate is 1.5. In this configuration, the thickness of the TiO_2 layer against the substrate is 102 nm, the thickness of the SiO_2 layer is 120 nm, and the thickness of the outer TiO_2 layer is 114 nm. The reflected light intensity for light incident
35 perpendicularly to the substrate at a wavelength of 635 nm is essentially zero.

40 Figure 4 illustrates one embodiment of a sensing system 100 incorporating the improved optical sensor 50 described above. Sensing system 100 includes a monochromatic light source 102, such as a laser, that produces light beam 24
45 incident upon diffuser 105. Other light sources are suitable including a monochromatic light bulb such as a mercury lamp, a filtered light emitting diode,
30 a white light source coupled with a filter, etc. Diffuser 105 diffuses light beam 24

5 such that light 110 is incident upon sensor 50 at a variety of angles. In one embodiment, the sample includes material for diffusing the light beam incident upon the sensor such that a separate diffuser is not needed. Depending upon the
10 angle of incidence and corresponding resonance angles of sensor 50, light 110 is transmitted through sample 21, sensor 50 and illuminates polarizer 114 that
5 transmits polarized light beam 117 having a electric vector parallel or perpendicular to the grooves of the surface of sensor 50.

15 Lens 115 focuses polarized light 117 to a corresponding point along detector array 120. In other words, polarized light 117 enters lens 115 at a
10 variety of angles and is focused along detector array 120 according to the angle. Detector array 120 outputs a signal that indicates corresponding intensities of the
20 light focused along detector array 120. Based on the signal, controller 122 determines one or more resonance angles and calculates a measure of the targeted substance in the sample. This configuration is particularly advantageous in the
25 sense that no moving parts are required. In one embodiment, controller 122 sounds an alarm when the calculated measure of targeted substance 18 exceeds a predetermined threshold. After sensing is complete, sensor 50 may be disposed
30 or may be washed and reused.

Several embodiments of an optical assaying method and apparatus have
20 been described. In one aspect, the present invention is an optical sensor having dielectric film stack that includes a plurality of dielectric layers. Each dielectric
35 layer comprises a dielectric material selected from a first dielectric material having a first index of refraction and a second dielectric material having a second index of refraction. In one embodiment, the dielectric film stack is formed such that the
40 dielectric material of the dielectric layers alternates between the first dielectric material and the second dielectric material. The dielectric film stack is either
25 formed as a dielectric mirror such that light incident upon the sensor reflects from the sensor or as an anti-reflection film stack such that light incident upon the light
45 beam propagates through the sensor.

30 The inventive sensor is easily manufactured such that the resonance angles can easily be tuned yet overcomes the limitations of grating-based SPR sensors.

5 More specifically, the inventive sensor uses a dielectric film stack instead of a thin
metal film. The inventive sensor exhibits a resonance that is comparable in
10 magnitude with resonances commonly exhibited by conventional SPR sensors.
However, unlike grating-based SPR sensors, a sample may be assayed by
5 reflectance from the substrate side without propagating light through the sample.
In addition, the sensor allows a sample to be assayed with transmitted light. One
15 advantage of assaying with transmitted light is the ability to use a diffused light
source. In addition, because the sensor does not rely on the use of conductive
metals, the sensor enables sharp resonances at shorter wavelengths than
10 conventional SPR sensors.

Claims

5

10

15

20

25

30

35

40

45

50

55

5

We claim:

10

1. A sensor for optically assaying a substance in a sample, wherein the sensor comprises a dielectric film stack having a plurality of dielectric layers, and further wherein for at least one angle of incidence the dielectric layers operate as a waveguide for light incident upon the sensor.

15

2. A sensing system, comprising:
 - a light source generating light;
 - a sensor comprising a stack of dielectric layers, wherein the sensor receives the light and for at least one angle of incidence the dielectric film stack operates as a waveguide such that a portion of the light propagates within the dielectric layers;
 - a detector receiving light from the sensor and producing an output signal as a function of an intensity of the light; and
 - a controller coupled to the detector for calculating a measure of the substance in the sample as a function of the output signal.

30

35

3. The article of claim 1, wherein the dielectric film stack is formed outwardly from a substrate having a grooved surface.

40

4. The article of claims 1 or 2, wherein at least two of the dielectric layers comprise a dielectric material selected from a first dielectric material and a second dielectric material, wherein the first dielectric material has a first index of refraction and the second dielectric material has a second index of refraction, and wherein the dielectric film stack is formed such that the dielectric material of the dielectric layers alternates between the first dielectric material and the second dielectric material.

45

50

55

- 5 5. The article of claims 1 or 2, wherein the dielectric film stack is formed as
a dielectric mirror such that the light incident upon the sensor reflects
10 from the sensor when the dielectric film stack is not operating as a
waveguide.
- 15 6. The article of claim 5, wherein the dielectric film stack is formed such that
when the dielectric film stack operates as a waveguide the reflected light
exhibits an attenuation of substantially at least 50%.
- 20 7. The article of claims 1 or 2, wherein the dielectric film stack is formed as
an anti-reflection film stack such that the incident light passes through the
25 sensor when the dielectric film stack is not operating as a waveguide, and
the transmitted light exhibits an attenuation of substantially at least 50%
when the dielectric film stack is operating as a waveguide.
- 30 8. The article of claim 4, wherein the first index of refraction is substantially
no greater than 1.8, and further wherein the second index of refraction is
substantially no less than 2.2.
- 35 9. The article of claim 4, wherein the first dielectric material is silicon
dioxide and the second dielectric material is titanium dioxide.
- 40 10. The article of claim 2, wherein the light source includes a diffuser for
diffusing light beam incident upon the sensor, wherein the sensing system
further includes a polarizer for polarizing light received by the detector,
and wherein the light source is a monochromatic light source.
- 45 11. A method for assaying a sample comprising:
interacting a sensor with a sample having a targeted substance,
wherein the sensor comprises a dielectric film stack having a plurality of
- 50
- 55

5

dielectric layers, and further wherein for at least one angle of incidence the dielectric film stack operates as a waveguide for light incident;

10

determining a measure of the targeted substance in the sample as a function of a detected optical anomaly exhibited by light received from the sensor.

15

12. The method of claim 11, wherein determining the measure includes detecting an optical anomaly in light reflected by or transmitted through the sensor.

20

13. The method of claim 11, wherein determining the measure includes illuminating the sensor with diffused light and detecting an optical anomaly in light transmitted through the sensor by focusing the transmitted light onto a detector array according to a transmission angle of the transmitted light.

25

30

35

40

45

50

55

AMENDED CLAIMS

[received by the International Bureau on 24 February 2000 (24.02.00);
original claims 1, 2 and 11 amended; original claim 3 cancelled;
remaining claims unchanged (3 pages)]

1. A sensor for optically assaying a substance in a sample, comprising:
a substrate having a grooved surface; and
a dielectric film stack formed outwardly from the substrate, wherein the
dielectric film stack includes a plurality of dielectric layers, and
further wherein for at least one angle of incidence the dielectric
layers operate as a waveguide for light incident upon the sensor.
2. A sensing system, comprising:
a light source generating light;
a sensor comprising a stack of dielectric layers formed on a substrate
having a grooved surface, wherein the sensor receives the light
and for at least one angle of incidence the dielectric film stack
operates as a waveguide such that a portion of the light
propagates within the dielectric layers;
a detector receiving light from the sensor and producing an output signal
as a function of an intensity of the light; and
a controller coupled to the detector for calculating a measure of the
substance in the sample as a function of the output signal.
3. [CANCELLED.]
4. The article of claims 1 or 2, wherein at least two of the dielectric layers
comprise a dielectric material selected from a first dielectric material and a
second dielectric material, wherein the first dielectric material has a first
index of refraction and the second dielectric material has a second index
of refraction, and wherein the dielectric film stack is formed such that the
dielectric material of the dielectric layers alternates between the first
dielectric material and the second dielectric material.

- 5
- 10
- 15
- 20
- 25
- 30
- 35
- 40
- 45
- 50
- 55
5. The article of claims 1 or 2, wherein the dielectric film stack is formed as a dielectric mirror such that the light incident upon the sensor reflects from the sensor when the dielectric film stack is not operating as a waveguide.
 6. The article of claim 5, wherein the dielectric film stack is formed such that when the dielectric film stack operates as a waveguide the reflected light exhibits an attenuation of substantially at least 50%.
 7. The article of claims 1 or 2, wherein the dielectric film stack is formed as an anti-reflection film stack such that the incident light passes through the sensor when the dielectric film stack is not operating as a waveguide, and the transmitted light exhibits an attenuation of substantially at least 50% when the dielectric film stack is operating as a waveguide.
 8. The article of claim 4, wherein the first index of refraction is substantially no greater than 1.8, and further wherein the second index of refraction is substantially no less than 2.2.
 9. The article of claim 4, wherein the first dielectric material is silicon dioxide and the second dielectric material is titanium dioxide.
 10. The article of claim 2, wherein the light source includes a diffuser for diffusing light beam incident upon the sensor, wherein the sensing system further includes a polarizer for polarizing light received by the detector, and wherein the light source is a monochromatic light source.
 11. A method of assaying a sample, comprising:
interacting a sensor with a sample having a targeted substance, wherein the sensor comprises a dielectric film stack having a plurality of dielectric layers formed on a substrate having a grooved surface,

5 and further wherein for at least one angle of incidence the
dielectric film stack operates as a waveguide for incident light; and
10 determining a measure of the targeted substance in the sample as a
function of a detected optical anomaly exhibited by light received
from the sensor.

12. The method of claim 11, wherein determining the measure includes
15 detecting an optical anomaly in light reflected by or transmitted through
the sensor.

13. The method of claim 11, wherein determining the measure includes
20 illuminating the sensor with diffused light and detecting an optical
anomaly in light transmitted through the sensor by focusing the
transmitted light onto a detector array according to a transmission angle
25 of the transmitted light.

5

10

15

Statement under Article 19(1)

20

Independent claims 1, 2, and 11 have been amended to include the
recitation of dependent claim 3, which has been cancelled.

25

30

35

40

45

50

55

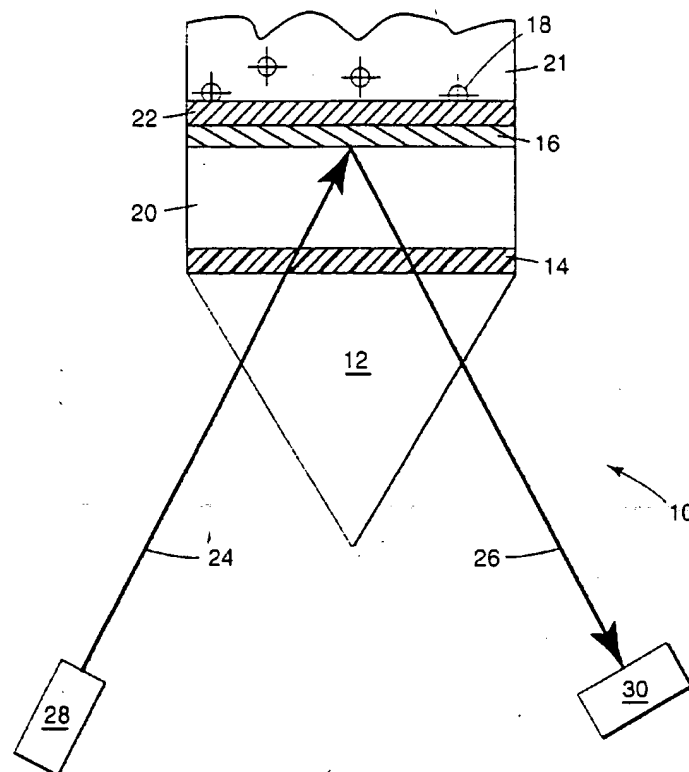


Fig. 1
Prior Art

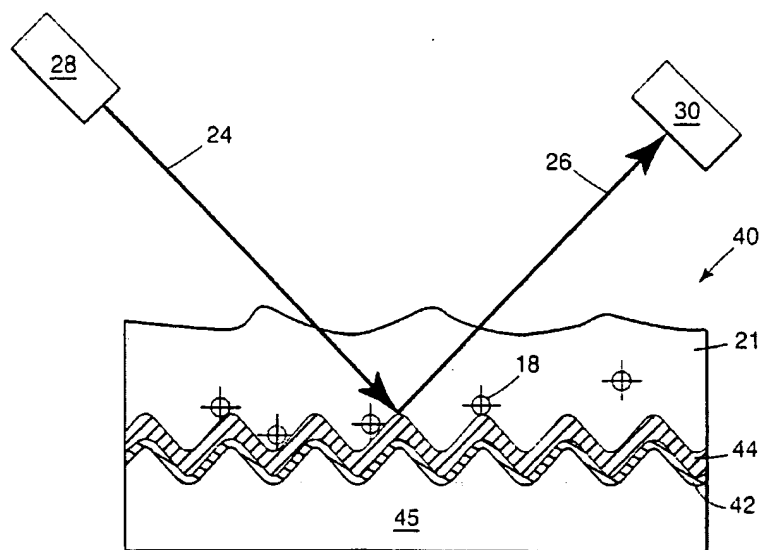


Fig. 2
Prior Art

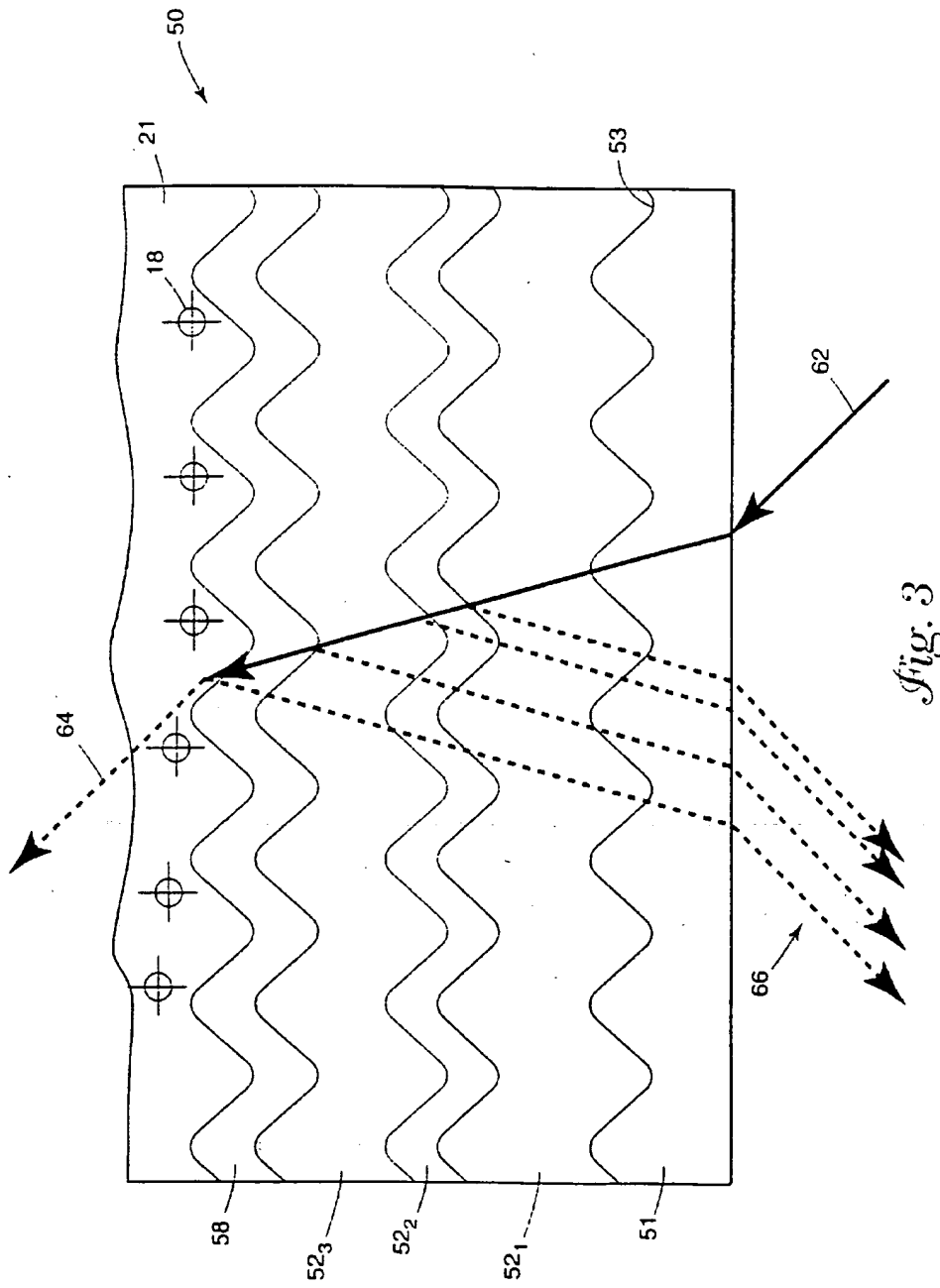
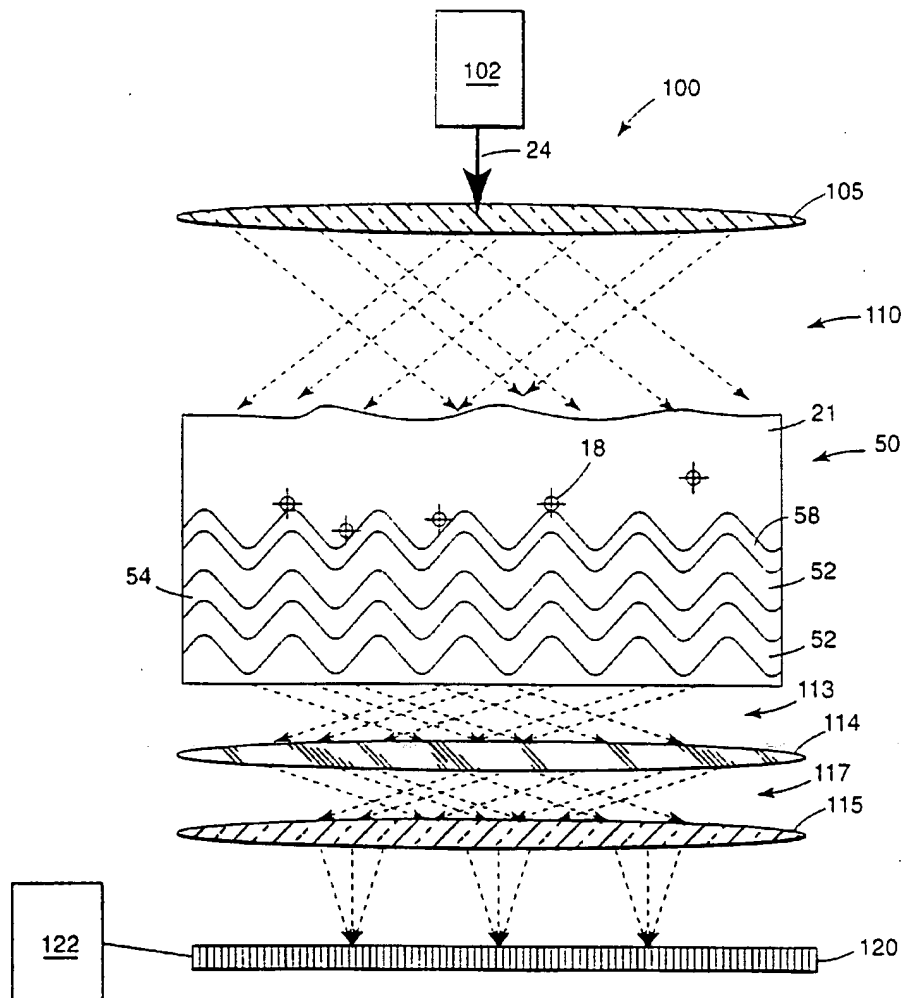


Fig. 3

*Fig. 4*

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/20689

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N21/77 G01N21/55

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 90 08313 A (PLESSEY OVERSEAS) 26 July 1990 (1990-07-26) page 3, line 1 - line 21 page 3, line 24 - page 4, line 2 page 5, line 14 - line 20 page 7, line 10 - line 13 page 8, line 7 - line 15 figures 1-3 --- -/-	1,3-8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

Special categories of cited documents:

- A* document defining the general state of the art which is not considered to be of particular relevance
- E* earlier document but published on or after the international filing date
- L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- O* document referring to an oral disclosure, use, exhibition or other means
- P* document published prior to the international filing date but later than the priority date claimed

- T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- S* document member of the same patent family

Date of the actual completion of the international search

17 December 1999

Date of mailing of the international search report

14/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Navas Montero, E

INTERNATIONAL SEARCH REPORT

Inter: nat Application No
PCT/US 99/20689

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
X	WO 95 33198 A (CIBA GEIGY AG :SCHOTT GLASWERKE (DE); ZEISS STIFTUNG (DE); DANIELZ) 7 December 1995 (1995-12-07)	1,3,4,9, 11
Y	page 1, line 12 - line 16 page 4, line 25 -page 5, line 10 page 13, line 11 - line 24 page 16, line 21 - line 24 page 17, line 23 - line 28 figure 1	10
Y	EP 0 455 067 A (HOFFMANN LA ROCHE) 6 November 1991 (1991-11-06) column 11, line 13 - line 15	10
X	WO 98 22807 A (CROSS GRAHAM HUGH :IMCO 1097 LTD (GB); FARFIELD SENSORS LTD (GB);) 28 May 1998 (1998-05-28) page 1, line 5 - line 13 page 4, line 30 - line 37 page 8, line 5 - line 12 page 9, line 17 - line 34 page 13, line 31 -page 14, line 7 figures 4,7	1-4,11
A	EP 0 596 421 A (HOFFMANN LA ROCHE) 11 May 1994 (1994-05-11) column 2, line 48 -column 3, line 17 column 13, line 38 - line 42	1,9
A	EP 0 175 585 A (CORNING GLASS WORKS) 26 March 1986 (1986-03-26) page 9, line 8 - line 21 page 12, line 26 -page 13, line 8 figures 1-3	1,4
A	WO 97 29362 A (THERMO FAST UK LIMITED LYNDIN NIKOLAI MIKHAILOVICH (RU); SYCHUGOV) 14 August 1997 (1997-08-14) page 6, line 4 - line 6	6,7

Form PCT/ISA210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No.

PCT/US 99/20689

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9008318 A	26-07-1990	GB 2227089 A EP 0404900 A	13-07-1990 02-01-1991
WO 9533198 A	07-12-1995	AT 172300 T AU 2317995 A AU 689604 B AU 2734695 A CA 2190362 A CN 1149335 A CN 1149336 A CZ 9603471 A CZ 9603472 A DE 69505370 D DE 69505370 T WO 9533197 A EP 0759159 A EP 0760944 A FI 964664 A FI 964684 A HU 76407 A HU 76406 A JP 10501616 T JP 10501617 T PL 317379 A PL 317402 A SK 151296 A SK 151396 A US 5959292 A US 5822472 A ZA 9504325 A ZA 9504327 A	15-10-1998 21-12-1995 02-04-1998 21-12-1995 07-12-1995 07-05-1997 07-05-1997 11-06-1997 12-03-1997 19-11-1998 01-04-1999 07-12-1995 26-02-1997 12-03-1997 24-01-1997 27-01-1997 28-08-1997 28-08-1997 10-02-1998 10-02-1998 01-04-1997 14-04-1997 09-07-1997 09-07-1997 28-09-1999 13-10-1998 27-11-1995 27-11-1995
EP 0455067 A	06-11-1991	CA 2041438 A JP 5346398 A US 5455178 A	04-11-1991 27-12-1993 03-10-1995
WO 9822807 A	28-05-1998	EP 0939897 A	08-09-1999
EP 0596421 A	11-05-1994	CA 2108705 A JP 6265553 A	07-05-1994 22-09-1994
EP 0175585 A	26-03-1986	AT 67857 T AU 583053 B AU 4763985 A CA 1266998 A CA 1269546 A DE 3584210 A JP 1953760 C JP 6064063 B JP 61089528 A US 4880752 A	15-10-1991 20-04-1989 27-03-1986 27-03-1990 29-05-1990 31-10-1991 28-07-1995 22-08-1994 07-05-1986 14-11-1989
WO 9729362 A	14-08-1997	EP 0879411 A	25-11-1998